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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/674,935	12/21/2000	Timothy Raymond Hirst	9274	8699

7590 06/15/2006

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EXAMINER	
HINES, JANA A	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 06/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/674,935	HIRST ET AL.	
	Examiner	Art Unit	
	Ja-Na Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 April 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38-53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38-53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry

1. The amendments entered January 30, 2006 and April 3, 2006 have been entered. Claims 38 and 49 have been amended. Claims 1-37 have been cancelled. Claims 38-53 are under consideration in this office action.

Withdrawal of Rejections

2. The following rejections have been withdrawn:

a) The objection of claim 1 and the specification;

b) The rejection of claims 1 and 3-5 under 35 U.S.C. 112, second paragraph;

c) The rejection of claim 1 under 35 U.S.C. 102(b) as being anticipated by Williams et al., (WO 97/02045);

d) The rejection of claims 1 and 3-5 under 35 U.S.C. 102(b) as being anticipated by Hazama et al., (Immunology, 1993).

Response to Arguments

3. Applicants' arguments with respect to claims 1 and 3-5 have been considered but are moot in view of the new ground(s) of rejection.

New Grounds of Rejection

Claim Objections

4. Claim 43 is objected to because of the following informalities: Claim 43 ends with a comma and not a period. Appropriate correction is required.

Claims 45 and 48 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Dependant claim 45 is drawn to co-administration of the EtxB and the antigen, however claim 43 already recites administration of the EtxB in conjunction with an antigen. Therefore, appropriate clarification is required to overcome the objection. Similarly, claim 48 has the same issue.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 38-53 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "enhancing the level of an immune response" in the claims is a relative; more specifically the term “enhancing” renders the claim indefinite. Applicants' assert that the term is commonly employed and that there is no absolute standard.

Therefore it is the examiner's position that the claims are indefinite because the claims do not refer to any type of comparison. The claims broadly recite enhanced immune response and are not limited to the levels of B and T cells. The phrase is not defined by the claim, nor does the specification provide a standard for ascertaining the requisite degree of enhancement. It is the examiner's position that one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Moreover, there is no disclosure of what the baseline level of an immune response should be which in-turn allows one to know when an enhanced level is reached. There is no comparison in the specification of a mammal's enhanced immune response when it received the EtxB and when it did not. Thus the metes and bounds of the phrase cannot be ascertained and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention with respect to this enhanced level of an immune response. Thus, applicants' arguments are not persuasive and the rejection is maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 38-39, 43-45 and 49 are rejected under 35 U.S.C. 102(b) as being anticipated by Williams et al., (WO 97/02045) published January 23, 1997. The claim is drawn to a method for enhancing the level of an immune response to a vaccine against

an infectious agent in a mammalian subject comprising administering to the subject an effective amount of the B subunit of *Escherichia coli* heat labile enterotoxin (ExtB) wherein the EtxB is free from whole toxin and not linked to an antigen.

Williams et al., teach therapeutic agents for use in the treatment of mammalian diseases (page 1, line 35 – page 2, line 2). The basis of the invention is that the pure B-subunit of *E.coli* heat labile enterotoxin (ExtB) binds to receptors found on the surface of mammalian cells and this binding induces differential immune response effects on lymphocytes including activation of B and T cells (page 2, lines 1-5). The acronym ExtB means the pure B subunit of *E.coli* heat labile enterotoxin (page 1, lines 34-36). Williams et al., teach separate administration of the therapeutic agent, which is ExtB and the antigenic determinant so as to enable separate administration of the moieties (pages 3-4, lines 5-3). The ExtB has already been suggested as a vaccine carrier because of its ability to modulate lymphocyte populations (page 10, lines 9-13). Williams et al., teach co-administration and separate administration which occur at the same time (page 8, lines 7-13). Williams et al., teach that the wild type and mutant forms of ExtB have binding capabilities and are known immunomodulators (page 11, line 31- page 12, line 5). Williams et al., teach the administration of EtxB or ExtB mutants to mice (page 14, lines 25-27). The results were expressed as mean IgG and IgA antibody titers in serum, wherein the results indicated an enhanced immune response by the antibodies, see Figure 2. Figure 3 teaches the kinetics of lymphocyte proliferation where the mice were injected with 30ug of a mutant version of ExtB (page 14, line 35- page 15 line 10). The injected amounts of ExtB are effective to enhance the

level of the immune response, just as required by the claims. Figure 4 teaches that immunization with either pure or mutated ExtB caused an increased activation in B cells. Therefore Williams et al., teach administering to the subject an effective amount of the ExtB wherein the ExtB is free from whole toxin and not linked to an antigen.

Accordingly, Williams et al., clearly teach a method for enhancing the level of an immune response to a vaccine against an infectious agent in a mammalian subject comprising administering to the subject an effective amount of the B subunit of *E.coli* heat labile enterotoxin (ExtB) wherein the EtxB is free from whole toxin and not linked to an antigen just as required by the instant claims.

7. Claims 38-53 are rejected under 35 U.S.C. 102(b) as being anticipated by Hazama et al., (Immunology, 1993).

The claims drawn to a method for enhancing the level of an immune response to a vaccine against an infectious agent in a mammalian subject comprising administering to the subject an effective amount of the B subunit of *Escherichia coli* heat labile enterotoxin (ExtB) wherein the EtxB is free from whole toxin and not linked to an antigen. The dependant claims are drawn to the vaccine being one for an infectious agent that is a member of the herpes virus family and selected from the group consisting of at least Herpes Simplex Virus –1 (HSV-1).

Hazama et al., teach that the non-toxic B subunit (LTB) of the heat labile toxin produced by enterotoxigenic *Escherichia coli* has been expected to potentiate local IgA antibody response to co-administered foreign antigens (page 643 para. 2). The LTB of

Hazama et al., is same B subunit of the heat labile *Escherichia coli* enterotoxin referred to by the instant claims as ExtB. In this study Hazama et al., created a recombinant LTB (ExtB) and investigated the mouse mucosal and systemic immune response elicited by intranasal immunization with several forms of a recombinant viral antigen (page 644, para. 2). These immunizations included the use of truncated Herpes Simplex Virus Type 1 (HSV-1) glycoprotein D (t-gD) being co-administered with LTB (page 644, para. 2). Therefore Hazama et al., teach administering to the mammalian mouse subject an effective amount of the LTB wherein the LTB is free from whole toxin and not linked to an antigen, just as required by the claims. Furthermore, Hazama et al., teach co-administration, just as required by the claims. Hazama et al., also teach the measurement of the antibody response, see Table 1 (page 646), which shows the administration of effective amounts of LTB alone and the co-administration of t-gD and LTB. Thus the injected amounts of LTB are at an amount effective to enhance the level of an immune response, just as required by the claims. The LTB by itself exhibited high immunogenicity when administered (page 647, para. 2). Table 2, at page 646, shows protection against a HSV-1 challenge in mice while table 4 shows protective immunity against HSV systemic infection in mice. The glycoproteins of HSV are vaccines against HSV-1 infectious agents, see the instant specification at example 1 (pages 33-34), example 4 (page 35), and example 7 (pages 36-37) which teach that these same HSV-1 glycoproteins are vaccines against HSV infections.

Therefore Hazama et al., teach a method for enhancing the level of an immune response to a glycoprotein vaccine against a HSV-1 infectious agent in a mouse subject

comprising administering to the subject an effective amount of the B subunit of *E.coli* heat labile enterotoxin (ExtB) as known as LTB wherein the EtxB or LTB is free from whole toxin and not linked to an antigen just as required by the instant claims.

Response to Arguments

8. The rejection of under 35 U.S.C. 102(b) as being anticipated by Williams et al., (WO 97/02045) is maintained. Applicants' urge that Williams is drawn to treating autoimmune disease and does not teach protection against infectious diseases. In response to applicant's argument that Williams is not drawn to infectious diseases, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. Here there is no difference between the administration of the exact same ExtB in a therapeutically effective amount as taught by Williams et al., and the instant claims.

In response to applicant's arguments, the recitation of a method of enhancing an immune response in a mammal to a vaccine against infectious disease has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA

1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951). Furthermore, it is noted that the claims do not require the administration of the vaccine, rather the body of the claims simply requires the administration of the ExtB, thus Williams meets the limitations of the instant claims.

In response to applicant's argument that Williams et al., is drawn to treating autoimmune disease and does not teach protection against infectious diseases, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be inherent. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). Therefore, applicants' arguments are not persuasive.

9. The rejection under 35 U.S.C. 102(b) as being anticipated by Hazama et al., (Immunology, 1993) is maintained. Applicants' assert that the administration taught by Hazama et al., reports a low level increased immune response. However it is the examiner's position that Hazama et al., teach an increase, which is all that is required of the claims. The fact that Hazama et al., disclose results which show that other administrations resulted in higher enhanced immune levels does not distinguish the instant claims over this art. The disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. *In re Susi*, 440 F.2d 442, 169 USPQ 423 (CCPA 1971). "A known or obvious composition does not become patentable simply because it has been described as somewhat

inferior to some other product for the same use." *In re Gurley*, 27 F.3d 551, 554, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994). Furthermore, "[t]he prior art's mere disclosure of more than one alternative does not constitute a teaching away from any of these alternatives...." *In re Fulton*, 391 F.3d 1195, 1201, 73 USPQ2d 1141, 1146 (Fed. Cir. 2004).

Therefore, the level of significant mucosal immune response or the failing to provide protective immunity of the HSV-1 disease, does not teach away from the instant claims. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies i.e., a specific level of enhanced immune response or the failing to produce protective immunity are not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). There is no requirement of a specific level of enhancement. And there is no requirement that the instant claimed method protect against the infectious disease. Rather the claims simply require administering to a mammal at an effective amount of the B subunit of *E.coli* heat labile enterotoxin (ExtB) as known as LTB wherein the EtxB or LTB is free from whole toxin and not linked to an antigen wherein the administration increase the levels of B and T cell lymphocyte response. Applicants' refer to the activity of the fusion protein as a basis for a teaching away, however Hazama et al., teach more than just the fusion protein, it teaches separate proteins an co-administration. Hazama et al., states that tgD-LTB co administered with LTB produced a 10-fold level higher level of serum

antibodies (page 648). Therefore, Hazama et al., teach all the limitations of the claims. Therefore contrary to applicants' argument, the prior art does not teach away from the instant claims, since the prior art teaches the exact same method step.

Conclusion

10. No claims allowed.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ja-Na Hines
June 6, 2006

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